UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Beth Fertich

From: Eric Bohnenblust, Ph.D., Entomologist

Secondary Review: Jennifer Saunders, Ph.D., Senior Biologist

Date: 2/9/2017

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

~~**THIS DER CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 437580
Decision no.: 523384
Submission no: 996736
Action code: R350.1
Product Name: Perimeter Plus Insect Guard
EPA Reg. No or File Symbol: 82392-3
Formulation Type: Treated Fabric
Ingredients statement from the label with PC codes included:
Etofenprox 0.90% PC: 128965
Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate): 0.207 mg etofenprox/cm^2 fabric
Use Patterns: Treated military uniforms for protection of covered skin from biting mosquitoes

I. Action Requested: Review 3 MRIDs: a response to a 10-day deficiency letter, rationale for bridging data with different fabrics, and rationale to bridge mosquito data to support sand flies and black flies.

II. Background: On December 15, 2016, EPA sent the registrant a 10-day deficiency letter associated with OPP decision No. 523384. The letter stated that there is no rationale or data for bridging data collected with military clothing to support all fabric types, and no data to support the addition of public health species other than mosquitoes. The registrant submitted a rebuttal to the deficiency letter consisting of three MRIDs, including a response to the 10-day letter and two bridging rationales.

III. MRID Summary:

50136701. PERIMETER PLUS INSECT GUARD: Registrant's Responses to 10-Day Deficiency Letter from the EPA Dated December 15, 2016.

(1) This MRID contains a paragraph noting that the pertinent responses to the deficiencies noted in the 10-day letter are contained in MRIDs 50136702 and 50136703. No data or bridging arguments are contained in this MRID.

(2) **Conclusion: Supplemental.** This MRID refers to the bridging arguments found in MRIDs 50136702 and 50136703. Please see the reviews for those MRIDs below.

50136702. Rationale for Bridging Data Collected with Military Fabric to Other Fabric Types.

(1) GLP standards are not applicable to this bridging argument.

(2) **Summary Rebuttal Points and EPA Responses:**

Registrant Point 1: The manufacturing process for etofenprox treated clothing is unique and is the same for all fabric types. However, as described in the EPA accepted manufacturing process, the time needed to wet the fabric and the total quantity of insecticide added to the treatment mixture will vary with fabric weight and type in order to attain the nominal concentration of 0.9% w/w.

EPA Response: The Agency acknowledges that the process for treating clothing with etofenprox is unique and that all fabrics are treated using the same method.

Registrant Point 2: When evaluating the fabric treatment for registration/regulatory studies, the fabric type chosen to evaluate efficacy and wash duration is the fabric type that is the most difficult treat and bind the polymerized etofenprox to. The Flame Resistant Army Combat Uniform (FRACU) was chosen for these evaluations because it is the most difficult fabric to treat due to its fire resistant properties and additives when compared to any other fabric. The interstitial spaces between the fabric threads are also larger when compared to other fabrics, making it easier for mosquitoes to bite through. Use of this fabric as the surrogate for other fabrics was also discussed with the EPA Registration Division (RD) and Human Health Effects Division (HED) in various meetings in 2013 and 2014 and the EPA Human Studies Review Board (HSRB) in the April 2014 and October 2015 meetings. The RD, HED and the HSRB all agreed with this approach to evaluation, and agreed if bite protection studies were successful with this fabric type over washing up to 75x, the etofenprox will repel/kill mosquitoes from all other fabric types as long as it is treated to achieve 0.9% w/w + 10% because the amount of etofenprox needed to provide bite protection will be available on the surface of the treated fabric (0.207 mg/cm2). The etofenprox bite protection assay conducted with etofenprox treated FRACU fabric (MRID 49684002) showed over 90% bite protection up to 75 washes; therefore, as per discussions with RD, HED and the HSRB we believe we can bridge this data to all other fabrics. Skin irritation was also evaluated with etofenprox treated FRACU fabric at up to 10x the product concentration (MRID 49684003) and there was no skin irritation observed under wet, dry, or sweat simulated conditions in testing using a protocol approved by EPA.

EPA Response: The minutes for the April 2014 HSRB meeting when the protocol was reviewed reference the phrase "The data also will provide value through the improved ability to register products, such as military clothing, with EPA." There is no evidence to suggest that fabric types other than "military clothing" were discussed. The minutes for the October 2015 meeting reference the fabric type that the data submitted may support and are specific to "etofenprox-treated uniforms." Also, in the HSRB final report for the October 2015 meeting, the report mentions "impregnated fabric" numerous times; however, the final report is written by the board and this appears to be inexact wording because the purpose as stated by the HSRB was "to determine the bite protection level of the etofenprox-treated U.S. military Fire Resistant Army Combat Uniforms (FRACUs)." Importantly HSRB only makes recommendations to EPA on whether the study is scientifically and ethically sound; the board does not make any direct decisions with regard to specifically what claims, use patterns, or fabric types are supported on the label. Therefore, there is no direct evidence in the meeting minutes from either HSRB meeting to indicate that the discussion regarding fabric type included consumer products such as denim jeans, cotton t-shirts, yoga pants, etc. We have also reviewed the meeting minutes from pre-registration meetings with the registrant and in the meeting minutes available to the reviewer (minutes from all pre-registration meetings could not be found), there is no indication of discussion regarding testing FRACU uniforms and bridging the data to support consumer products. All discussions appear to have centered around the FRACU as the worst case scenario with regard to impregnated military uniforms. In one meeting, there was a reference stating that interest in a claim against black flies would only be of interest for consumer products; however, there are no other references to consumer products. Moreover, the titles and purpose of the protocol and study were to determine bite protection efficacy for the military and

military uniforms, suggesting that there was no intention of using the study to support efficacy for consumer products. The registrant does not in this MRID provide any direct evidence of discussion or agreement by the Agency with regard to using data collected testing FRACU uniforms to support efficacy of consumer clothing against public health pests. Clothing can be made from various fabrics of different densities, weaves (looser or tighter), thickness, etc., and thus, efficacy and duration of efficacy for all fabrics are unlikely to be the same. The Agency will consider bridging data collected on the FRACU to consumer fabrics on a case by case basis; however, bridging will be considered for specific methods of impregnation on the basis of physical properties for individual fabrics (e.g., densities, thickness, tightness of weave, type of material).

Registrant Point 3: This practice of evaluating FRACU garments/fabric has been applied to permethrin treated fabrics and the data bridged to all other fabric types and articles. Pine Belt Processing received approval for amendment to their uniform label to add permethrin treated fabrics and articles in April 2016 (EPA Reg. No. 82392-1). EPA has approved this practice for other registrants as well based on permethrin treated clothing labels and remains confident in its use because Insect Shield has been allowed to receive clothing and articles from consumers for treatment to 0.52% (w/w) permethrin at their factory. Factory treated consumer owned garments/articles are shipped back to owners to wear as protection against bites from arthropod disease vectors. When EPA issued a product specific data call-in for products used to treat permethrin fabric treatment, it was to determine if the treatment processes used for registrants' products were equivalent and capable of achieving the bite protection and wash longevity claimed on the label. This was based on the fact that the DoD had reported publicly that different treatment process provided different bite protection levels and treatment residuality on FRACU fabric - despite EPA allowing "me-too" registrants based on 0.52% permethrin w/w only. As a result, DoD began evaluating all products even though they all contained 0.52% permethrin w/w.

EPA Response: The EPA acknowledges previously bridging data collected on military fabrics to support other treated fabric products in the past, however, all fabric types may not equally protect people from mosquito bites and the Agency does not have data showing performance of all treated fabric types. In addition to the potential issue surrounding different treatment processes, the physical properties of different fabrics are likely to result in differences in how fabrics age and retain pesticides after laundering. Thus all treated fabrics, even when using a single application process, may not age equally or provide equivalent bite protection after a set number of washes. The Agency does not intend to bridge data collected testing FRACUs to support efficacy for consumer products without data or a case-by-case justification.

(4) **Conclusion: Supplemental.** The bridging argument presented in this MRID is informative, however, no direct evidence was provided indicating that EPA had agreed to use the FRACU uniform fabric to support all fabric types. In addition, the registrant did not provide physical characteristics for any specific fabric types and how they compare to the FRACU.

50136703. Bridging Argument to Selectively Cite Mosquito Efficacy Data (MRID 49684002) (D429130) to Support the Addition of Sand Flies and Black Flies to the Perimeter/ETO Insect Guard Product Label.

(1) GLP standards are not applicable to this bridging argument.

(2) **Summary Registrant Point:** In April 2015, EPA held a meeting with DoD, USDA-ARS, and Landis International/Mitsui Chemicals Agro, Inc. to discuss efficacy data development and the necessity - or not – of conducting human subject research to determine the ability of etofenprox treated fabric to repel/kill biting arthropods (please see attached minutes). During that meeting the DoD and USDA-ARS stated that bite protection assays with sand flies, biting midges, and black flies cannot be conducted because the mouthparts of these species are too short to bite through the treated fabric. On page 4 of the minutes the participants agreed that the treated uniform will be protective against black flies because they cannot bite through the fabric. For the same reason, the meeting participants agreed that bite protection testing cannot be done with species other than mosquitoes as described on pages 4 – 7 of the minutes. Therefore, bite protection assays with these species will not be necessary and the use and exposure of human subjects cannot be justified to test repellency claims.

Based on the discussions with the EPA and testimony of DoD and USDA-ARS experts, Pinebelt Processing believes that citation of the etofenprox treated fabric bite protection study (MRID 49684002) previously accepted by the EPA and the HSRB should satisfy the product performance data requirements to support the

addition of sand flies, biting midges, and black flies to the product label. These flies have a small body size and are likely to be as susceptible as mosquitoes to the etofenprox treatment when landing and crawling on treated fabric. With their short mouthparts and legs they are likely to have more body surface in contact with the treated fabric when compared to mosquitoes. Mosquito bite protection in the cited USDA-ARS study accepted by the EPA was very high (> 90%) and most of the exposed mosquitoes were killed following a 15-minute exposure to the etofenprox treated sleeves when compared to the untreated control sleeves through 75 washes. More testing is unlikely to provide any new information, hence, it is not an efficient use of time and resources of the EPA, HSRB, and the registrants (Pine Belt and MCAG).

EPA Response: As mentioned by the registrant, sand flies, black flies, and biting midges cannot be used to test bite protection because their mouthparts are too short to bite through treated fabric. However, etofenprox does not act as a volatile repellent when impregnated on clothing and therefore, treated clothing will not "repel" these biting insects from or protect untreated skin in the same manner as a repellent like DEET. Because both treated and untreated uniforms act as a physical barrier against sand flies, black flies, and biting midges, the "repellency" effect (defined as bite protection) is not an effect from the pesticide. The potential benefit of wearing fabrics treated with etofenprox versus untreated fabric to protect against sand flies, black flies, and biting midges would be manifested as a knockdown or mortality effect after contact with the treated uniform. The knockdown/mortality effect would need to be sufficient to incapacitate black flies, sand flies, and biting midges exposed to treated fabric.

(3) **Conclusion: Unacceptable.** The bridging argument presented in MRID 50136703 is not acceptable because both untreated and treated fabrics act as a physical barrier against sand flies, black flies, and biting midges. The treated fabric may have a toxic effect after contact; however, that can be tested through contact bioassays conducted in the laboratory and would not require human studies. In addition, without data showing that treating fabrics with etofenprox has a pesticidal effect against sand flies, black flies, and biting midges, making efficacy claims against these species is misleading and encourages people to wear pesticide impregnated clothing which exposes them to pesticide residues in situations where there is no benefit to wearing pesticide impregnated clothing. Data showing efficacy against the aforementioned species should be submitted to support efficacy claims.

IV. EXECUTIVE DATA SUMMARY:

(A) The submitted bridging arguments do not support the numerous different fabric types and use patterns listed on the label. Bridging arguments should be made on a case by case basis and should include physical characteristics of the fabrics. The Agency will not directly bridge bite protection data collected with mosquitoes to support claims against sand flies, black flies, and biting midges because no evidence was presented to show that toxicity to etofenprox is similar between the mosquitoes and these additional fly species and "bite protection" is not an appropriate endpoint.

The proposed amended label for EPA Reg. No. 82392-3 also has claims of efficacy for up to 6 months for treated fabrics such as tenting, hunting blinds, truck covers, shelters, etc. In addition to some of the references (e.g., shelters) being vague and non-descript, many of these uses will result in situations where hunting blinds and truck covers, etc. are likely to be exposed to elements such as sunlight and precipitation continuously for long periods of time. Efficacy testing should be conducted with treated materials which are subjected to outdoor aging (direct sunlight and intermittent precipitation events) to determine the duration of efficacy against any claimed public health pests. In addition, many of these uses (e.g., hunting blinds and truck covers) are not intended to directly protect humans from biting insects, but instead are similar to residual surface sprays. Therefore, repellency claims are not appropriate for these uses and data submitted showing knockdown and subsequent mortality are most appropriate for these use patterns.

V. LABEL RECOMMENDATIONS:

(1) The addition of fabric types intended for consumer use are not supported.

(2) The following marketing claims are acceptable: No new efficacy claims are acceptable.

(3) The following marketing claims are unacceptable:
Repels sand flies, biting midges, and black flies
Repellency remains effective for 6 months of exposure to weathering for non-washable items (i.e., tents, shelters, truck covers, awnings, hunting blinds, kennel/stall coverings)

(4) The following MRIDs should be removed from the data matrix, as they are classified as “supplemental or unacceptable” to support the product: 50136701, 50136702, 50136703